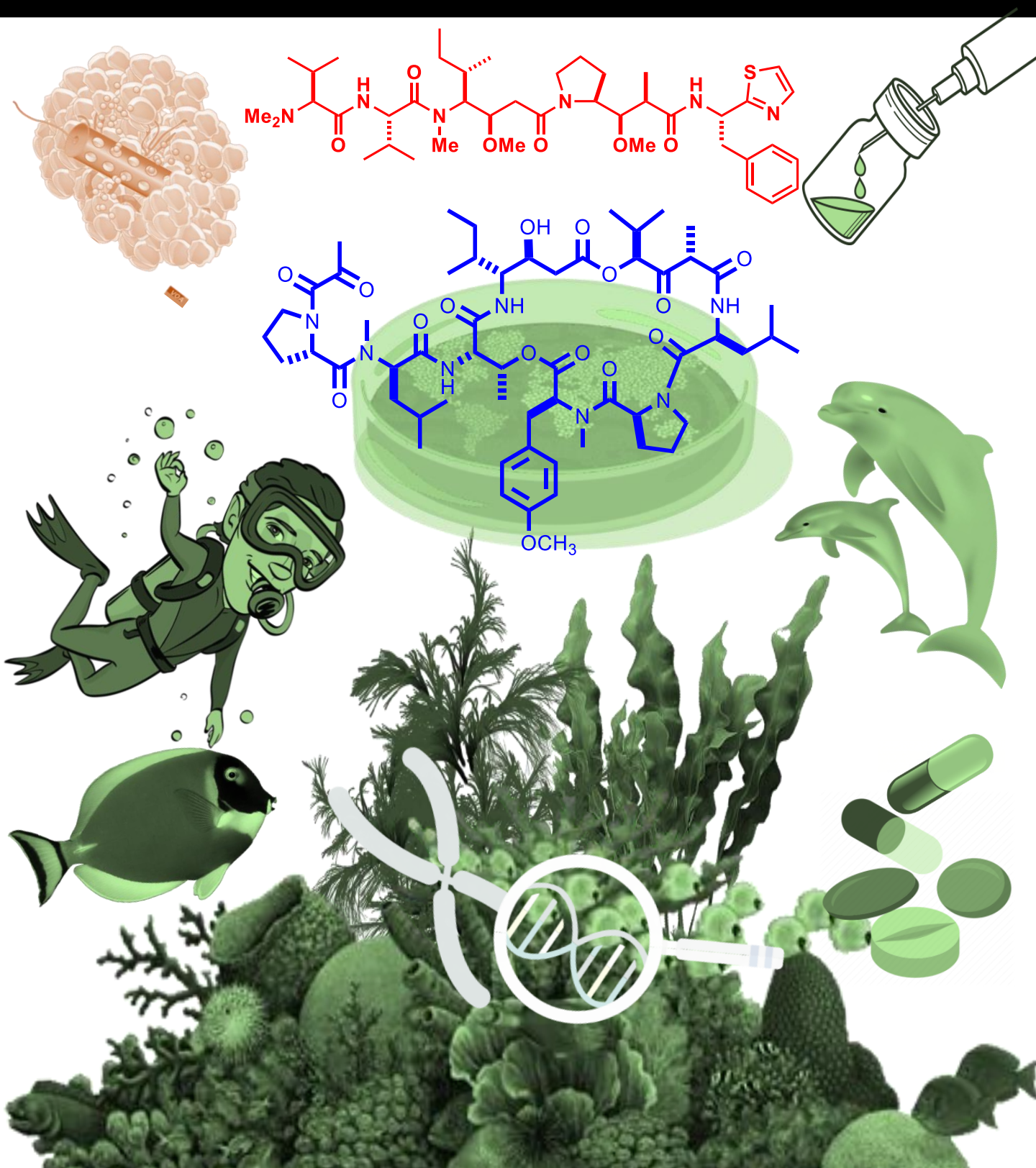


Marine Drugs

2021 – 2022 {Lecture 2}



Dr. Omar M. Sabry

Marine Drugs

❑ Marine Sample Collection

Samples of marine organisms near shores are collected by hand {intertidal} or by snorkeling.

Samples of marine organisms up to 100 feet can be done by SCUBA diving.

Samples of marine organisms more than 100 feet under water cannot be achieved by SCUBA, but using submarines {submersible}.

❑ Extraction of marine organisms

Marine creatures are keeping their pharmacologically active 2^{ry} metabolites inside their bodies to defend themselves from enemies. They are not secreting their bioactive constituents outside their bodies continuously. These 2^{ry} metabolic compounds are lipophilic {hydrophobic} compounds. During extraction step, sample homogenized then extracted with the suitable organic solvent e.g. ethanol, methanol, CH₂Cl₂, acetone and acetonitrile to dissolve the pharmacologically active organic compounds. If we use water for extraction, it will not dissolve these lipophilic bioactive compounds.

❑ Brine shrimp toxicity, ichthyotoxicity, fish toxicity

Brine shrimp toxicity or ichthyotoxicity {Snail killing activity} or even fish toxicity are important steps in isolation of bioactive marine Drugs. If the extract or the fraction is toxic to {Brine shrimp - snails - Gold fish}, extract must contain strong pharmacologically active compound{s} that is/are toxic in large dose. But when used in diluted concentration, it can treat certain ailments e.g. Sodium channel blockers in large dose can cause respiratory paralysis and death, but in small dose can be used as local anesthetic or pain killer in cancer chronic pains {e.g. Tetrodotoxin}.

❑ Bioassay-guided fractionation

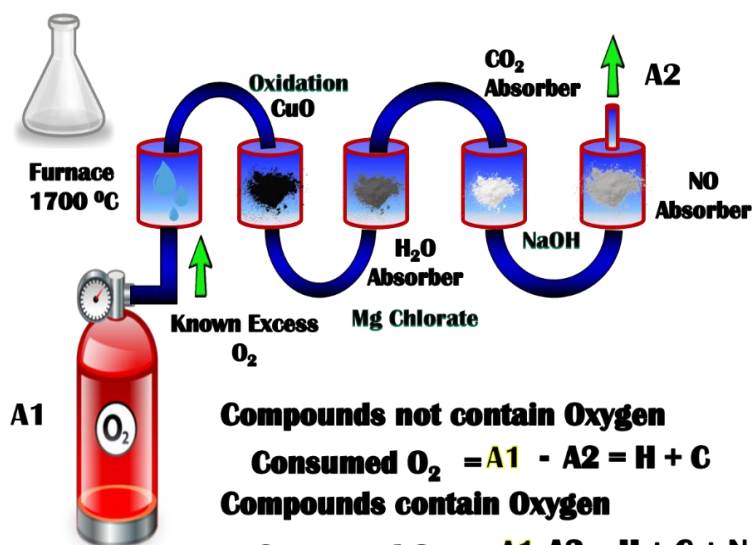
Bioassay-guided fractionation {e.g. Cytotoxicity – COX I inhibitory activity} as a useful technique in science of marine drugs involves testing the crude extract or preliminary fractions from chromatography in an assay or multiple assays e.g. cytotoxic activity and anti-inflammatory activity, determining what fractions or crude extracts show activity in the specific assays. Further fractionation of the active fractions or extracts is carried out and repeated where the new fractions are tested and the active fractions are further fractionated. This continues until the fraction only contains the bioactive pure compound.

❑ Structure Confirmation of Natural Products

After isolation and purification of the single pure compound by HPLC, structural elucidation of the bioactive compound can be performed using:

- **Elemental analysis:** Gives percentage elements in the compound e.g. % C, % O, % N, % H. Also gives us the molecular formula of the compound.

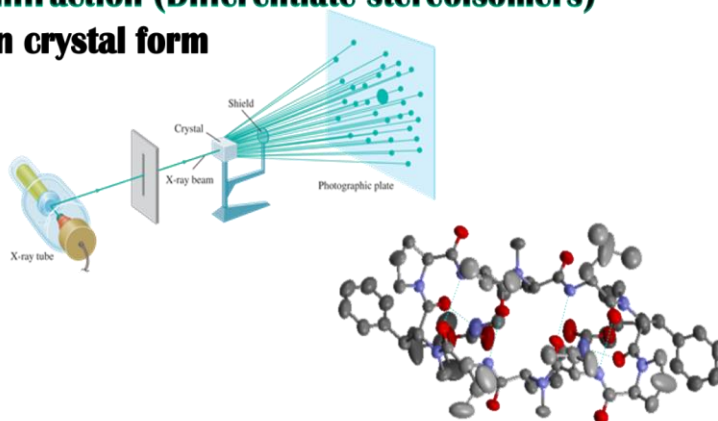
Elemental Analyzer



- **Ultraviolet-visible spectroscopy (UV-vis):** Gives an idea about the presence or absence of the conjugated unsaturated systems {double bonds}.
- **Infrared (IR) spectroscopy:** Gives an idea about the nucleus of the compound {fingerprint region}. Also gives an idea about functional groups e.g. OH, CH aromatic, C=O groups
- **MS spectroscopy:** Gives the molecular weight of the compound.
- **NMR spectroscopy:**
 - ^1H NMR** Gives us an idea about number and nature of the protons in the compound. e.g. Carboxylic protons, aldehydic protons, aromatic protons and aliphatic protons.
 - ^{13}C NMR** Gives us an idea about number and nature of the carbons in the compound. e.g. carbonyl carbons, Aromatic carbons, aliphatic carbons
- **X-ray Crystallography:** Can identify the compound and its stereochemistry if the compound is available in crystalline form.

X-Ray Spectroscopy

Identification of the 3D structure of any compound present in crystal form by X-Ray diffraction (Differentiate stereoisomers) in crystal form



☐ Many bioactive compounds fail to be medicine in clinical trials

To be approved as medicine, a compound can take about 30 – 40 year from its discovery to be in the market. A medicine can cost up to 1 billion dollars. Many marine natural compounds like Curacin-A and Kahalilide F failed in clinical trial phases as they may have unresolved problems in instability, insufficient supplying source, high toxicity and difficulty in total synthesis or semi-synthesis.

